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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,695	11/03/2005	Hesson Chung	HANO-003	1212

24353 7590 04/30/2008

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EXAMINER	
PALENIK, JEFFREY T	

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
04/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,695	CHUNG ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,10,11,16-19,22 and 38-43* is/are pending in the application.

4a) Of the above claim(s) *5 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,10,11,16-19 and 38-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3 Nov 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Remarks

The Examiner thanks the Applicants for their timely reply filed on 4 January 2008, in the matter of 10/521,695.

Applicants' arguments filed 4 January 2008 have been fully considered but they are not persuasive.

Applicants' election **with traverse** of Group I, claims 1-6, 10, 11, 16-19, 22 and 38-43, is acknowledged. Applicants traverse the restriction requirement citing MPEP §803 and stating that the search would not be "unduly burdensome."

Per PCT Rule 13.1, the international application shall relate to a group of inventions so linked as to form a single general inventive concept or a "unity of invention" (see MPEP 1850). Per PCT Rule 13.2, said "unity of invention" is fulfilled by defining a special technical feature that is shared amidst the claimed inventions. The Rule further specifies that "[t]he expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art."

Applicants' species elections: **triglyceride** as the oil species, **tricaprylin** as the particular oil species, **non-ionic surfactant** as the emulsifier species, **polyoxyethylene sorbitan (Tween)** as the particular emulsifier species, **insoluble drugs** as the additive species, **anticancer drugs** as the insoluble drug species, and **cisplatin** as the anticancer drug species, are also acknowledged. It is not explicitly stated in Applicants' response whether or not the species election is made with traversal. Since species traversal is not clear and no arguments are provided to traverse said species elections, the species elections are considered to be made **without traversal**.

Therefore, the requirement is deemed proper and is made **FINAL**.

Claims 5 and 22 of the elected Group I are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention and species, there being no allowable generic or linking claim.

The remaining claims 1-4, 6, 10, 11, 16-19, and 38-43 are presented and represent all claims under consideration.

Information Disclosure Statement

An Information Disclosure Statement filed 3 November 2005 is acknowledged and has been reviewed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 6, 10, 11, 16-19, and 38-43 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 33, 42, 43, and 48-51 of copending Application No. 10/521,669. Although the conflicting claims are not identical, they are not patentably distinct from each other because the aforementioned claims of the '669 application, like the claims of the elected instant application, are drawn to a composition comprising similar ranges of a monoglyceride compound, an oil compound (e.g. tricaprylin), an emulsifier (e.g. Tween), paclitaxel and the insoluble anticancer drug cisplatin.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Specification

The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

Claim Objections

Claims 1, 2, 16 and 39 are objected to because of the following informalities: the claims use the tilda "~" symbol to represent the term "about." Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

> pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. As amended, the instant claim set recites the following potential limitation to the monoglyceride compound "a mixture of monoglycerides semi-synthesized from triglycerides of vegetable ***and*** animal oil." After carefully examining the instant disclosure, the examiner respectfully submits that support for this amendment is lacking and the addition of said limitation is new matter. Specifically, the limitation "a mixture of monoglycerides semi-synthesized from triglycerides of vegetable ***and*** animal oil" is not set forth in the instant specification. The specification, including page 7, lines 8-14, have been carefully reviewed and sufficient support for the limitation "a mixture of monoglycerides semi-synthesized from triglycerides of vegetable ***and*** animal oil" was not found. Although the examiner acknowledges that the limitation "a mixture of monoglycerides semi-synthesized from triglycerides of vegetable ***or*** animal oil" is set forth in the instant disclosure (pg. 7, lines 8-14), the "vegetable ***and*** animal oil" limitation was not found. Herein, for the purposes of examination on the merits, the limitation will be considered in terms of "or" rather than "and".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-3 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "a mixture of monoglycerides semi-synthesized from triglycerides of vegetable or animal oil" in claim 3 renders the limitation to a monoglyceride compound indefinite because it not clear specifically which oils the limitation speaks to or recites. Herein, for the purposes of examination on the merits, the Examiner interprets the limitation to read on such compounds as soybean oil, which is known in the art to be comprised of triglycerides such as linoleic, linolenic, oleic, stearic and palmitic acids.

Claim 40 recites the limitation "the method…" in the second line of the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 10, 11, 16 and 38-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Carrier et al. (WO 99/49848).

The instant claims are drawn to a paclitaxel composition which comprising percent weight ranges of paclitaxel, at least one monoglyceride, at least one oil, and at least one emulsifier. Dependent claims 2 and 3 further limit the monoglyceride compound. Dependent

claims 4 and 6 further limit the oil to the triglyceride tricaprylin, respectively, and per the above species elections. Dependent claims 10 and 11further limit the emulsifier compound to the non-ionic surfactant polyoxyethylene sorbitan (e.g. Tween), respectively, and per the above species election. Dependent claim 16 further limits claim 1 such that the composition additionally comprises another additive from about 0.01 to about 5% by weight. Dependent claims 38-43 all recite functional limitations which read on intended use of the instant composition, which do not further limit the composition itself and are therefore interpreted as reading only on the claimed composition. Additionally, the preamble to each of the instant claims recites "via intravesical administration" as a limitation of intended use. This limitation will be given consideration to the extent that it limits the instant paclitaxel composition to a liquid (i.e. injectible) composition.

Carrier et al. teach a pharmaceutical composition comprising an **anticancer drug** as an active ingredient dissolved in a carrier system comprising at least one hydrophobic component and at least one surfactant (claim 1). Example 5 teaches a specific embodiment comprising paclitaxel (1.4% by weight), the **emulsifier Tween** 80 (43% by weight), the **caprylic/capric triglyceride** Miglyol 812 (28.7% by weight), and **soybean oil, which is a monoglyceride semi-synthesized from triglycerides of vegetable oil** (3.6% by weight). Example 5 includes other additives such as linoleic acid, which is present at about 3.5% by weight.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

> having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 6, 10, 11, 16-19, and 38-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carrier et al. (WO 99/49848) in view of Jacob (U.S. Patent 6,218,367) and in further view of the product listing of MultiChem, Inc. and the DrugBank Database.

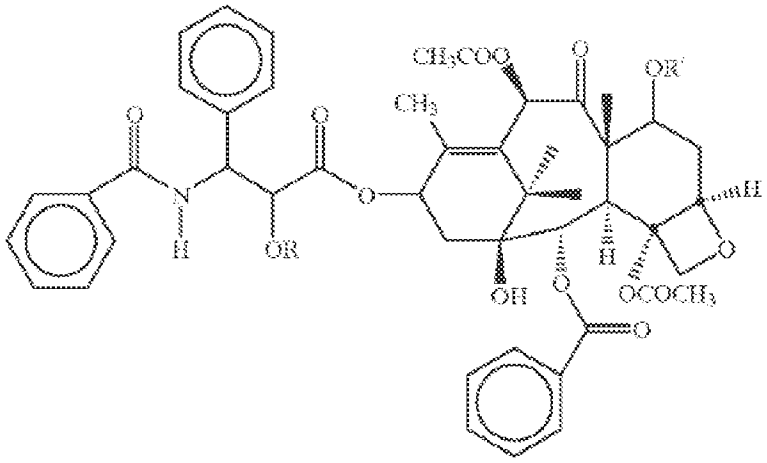
The instant claims are drawn to a paclitaxel composition, as described above. Dependent claim 6 further limits the triglyceride of claim 4 to the elected compound tricaprylin. Dependent claims 17-19 further limit the additive of claim 16 to the elected insoluble anticancer drug cisplatin.

The teachings of Carrier et al. are discussed above.

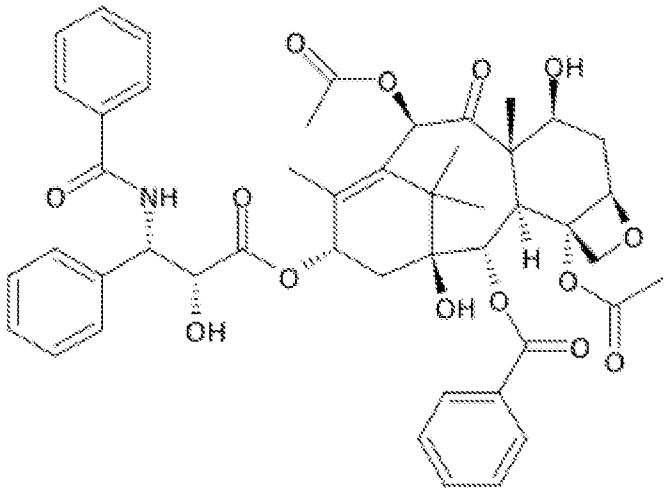
What Carrier is lacking are the teachings of **tricaprylin** and **cisplatin** as compounds of the instant paclitaxel composition.

Jacob teaches the following core compound Formula (I) in claim 1, which follows:

(I)



wherein both R and R' may be independently selected to be hydrogen, thus giving the formula for paclitaxel:



Paclitaxel

Jacob also teaches administration of an anti-tumor compound according to claim 1 (e.g. paclitaxel) in combination with **cisplatin** (claims 28). Various pharmaceutical dosage forms, both liquid and solid are taught in addition to administration routes (col. 7, lines 22-32).

Pharmaceutically acceptable carriers of the paclitaxel composition that are taught include: oils (e.g. fish oils), monoglycerides, **triglycerides** and emulsifiers (col. 7, lines 38-62).

In view of the combined teachings of the prior art, one of ordinary skill in the pharmaceutical art would have been motivated to prepare a paclitaxel composition comprising at least one emulsifier, monoglyceride, and **triglyceride**, in combination with the alkylating agent **cisplatin**, with a reasonable expectation of successfully obtaining a cellular-directed, anti-cancer pharmaceutical composition for treating male and female, reproductive- and bladder-based cancers. Such would have been obvious in the absence of evidence to the contrary since the online database DrugBank teaches that both paclitaxel and **cisplatin** are useful for the treatment of ovarian cancer, among other types, that both are capable as being administered intravenously and that they are both capable of having similar half-lives within the body. The DrugBank further teaches that paclitaxel interferes with gross, structural (e.g. microtubule), downstream cellular growth whereas **cisplatin** acts directly on the nuclear level, intercalating into a person's DNA to interfere with cellular division. Despite the fact that the two anti-cancer drugs target different levels and locations of the cellular reproduction cycle, the motivation to combine the two drugs remains for that very reason thereby resulting in the multi-faceted anti-neoplastic composition of the instant invention.

Neither of the references specifically teaches **tricaprylin** as the **triglyceride** compound nor **cisplatin** in the percent range, as claimed by the Applicants. The substitution of Miglyol 812 (e.g. **caprylic/capric triglyceride**), which is taught in Example 5 of Carrier et al., for the functionally equivalent compound **tricaprylin** (e.g. **glycerin tricaprylate or Miglyol 808**) as the **triglyceride** compound is well within the purview of the skilled artisan (see MultiChem, Inc.

reference). Given such properties of **cisplatin** such as high percentage of DNA protein binding and since the other pharmaceutically acceptable components which comprise the remainder of the paclitaxel composition are adjustable with respect to the claimed dosage form, it follows that a low percentage of **cisplatin** incorporated into the composition, such as that claimed by Applicants, is a result-effective parameter that a person having ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal **triglyceride** compound and optimal amount of anti-neoplastic alkylating agent to add to the dosage formulation in order to best achieve the cancer suppression results desired. Thus, absent some demonstration of unexpected results from the claimed parameters, optimization of the aforementioned constituents would have been obvious at the time of Applicant's invention.

No claims allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/
Examiner, Art Unit 1615

/M P WOODWARD/
Supervisory Patent Examiner, Art Unit 1615